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Carbon Tetrachloride: Position Document 1

(U.S.) Environmental Protection Agency
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16. Abstract (Limit: 200 words)

Preliminary Risk Assessment: Examination of possible unreasonable risks associated with uses of pesticide and a gathering of all available information to determine whether or not this or any other risk does exist. Initiates literature search and evaluates risk data. Limited information on exposure to forecast extent of risk.

17. Document Analysis a. Descriptors

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ENVIRONMENTAL PROTECTION AGENCY

[FRL ; OPP-30000/35A]

Carbon Tetrachloride

Pesticide Programs; Rebuttable Presumption Against Registration and Continued Registration of Certain Pesticide Products

AGENCY: Environmental Protection Agency (EPA).

ACTION: Carbon Tetrachloride - Position Document 1.

SUMMARY: Carbon tetrachloride (CCl_4) has been found to exceed certain risk criteria set forth in 40 CFR 162.11. This notice provides the Position Document 1 supporting the notice of rebuttable presumption against registration which is published elsewhere in this issue of the FEDERAL REGISTER. Registrants and other interested persons are requested to submit comments on the Position Document 1. This action is the first of several which will publicly report the Agency's progress in reviewing this chemical.

DATES: Rebuttal evidence and other information must be received on or before November 24, 1980.

COMMENTS: Written comments should be submitted to:

Document Control Officer,
Environmental Protection Agency,
Office of Pesticides and Toxic Substances (TS-793),
Room E-447,
401 M St. SW,
Washington, D.C. 20460.

EPA/OPP-80/107

FOR FURTHER INFORMATION CONTACT:

Jeff Kempter,
Environmental Protection Agency,
Special Pesticide Review Division (TS-791),
Office of Pesticide Programs,
RM. 711B, Crystal Mall #2,
401 M Street, SW,
Washington, D.C. 20460,
(703-557-7460).

SUPPLEMENTARY INFORMATION: Elsewhere in this issue of the FEDERAL REGISTER the notice of rebuttable presumption against registration has been issued. The Deputy Assistant Administrator, Office of Pesticide Programs, EPA, has determined that a rebuttal presumption exists against registration and continued registration of all pesticide products containing CCl_4.

Issuance of this RPAR means that potential adverse effects associated with the use of CCl_4 have been identified and will be examined further to determine if they do exist and, if so, whether they are unreasonable.

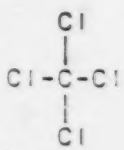
A position document on CCl_4 containing references, background information, and other material pertinent to the issuance of the rebuttable presumption against registration action has been prepared by the Agency and is published in this notice.

CARBON TETRACHLORIDE: POSITION DOCUMENT 1

BACKGROUND

A. Physical and Chemical Characteristic

1. Nomenclature. Carbon tetrachloride is a chlorinated hydrocarbon compound with the molecular formula CCl_4. Its structural formula is:



Other chemical names used by manufacturers are tetrachloromethane, perchloromethane, benzinoform, and tetrachlorocarbon.

2. Chemistry. CCl_4, a colorless liquid at room temperature, is prepared commercially by interaction of carbon disulfide and chlorine with a catalyst or by the chlorination of methane or higher hydrocarbons at 250° to 400°C. It has a moderately strong ethereal odor similar to that of chloroform and is miscible with alcohol, ether, benzene, chloroform, solvent naphtha, and most of the fixed and volatile oils. It is insoluble in water and is noncombustible.

CCl_4 has a molecular weight of 153.84, boiling point of 76.75°C, freezing point of -23°C, vapor pressure of 89.5 mm at 20°C, vapor density of 5.32 (air=1), and specific gravity of 1.585 at 25°C. One part per million (ppm) of CCl_4 is equivalent to 6.29 mg per cubic meter in air, and one mg/m^3 of

CCl_4 is equivalent to 0.159 ppm.

B. Registered Products and Uses

1. Products and production. There are currently 128 Federal pesticide registrations, held by 56 registrants, and 3 state registrations of products containing CCL_4 as an active ingredient. In addition, CCl_4 is registered as an inert ingredient in 15 products. Most of the registered products are mixtures of CCl_4 and other active ingredients such as ethylene dibromide, sulfur dioxide, and carbon disulfide.

Records indicate that nearly one billion lbs. of CCl_4 are produced in the U.S. annually. NIOSH (1975) reports 997 million lbs. for 1973, Johns (1976) reports 932.7 million lbs. for 1976, and USEPA (1977) reports 932.7 million lbs. for 1977. In 1973, 95 percent of this production was used in the manufacture of fluorocarbons.

The remaining 5 percent, or 49.5 million lbs., was formulated into pesticidal products, metal degreasers, dry cleaning solvents, refrigerants, propellants, fire extinguisher solutions and semiconductors.

The major domestic formulators of carbon tetrachloride are:

i. Allied Chemical Corporation: Moundsville, West Virginia.

ii. Dow Chemical USA: Freeport, Texas; Pittsburgh, California; Plaquemine, Louisiana.

iii. E. I. Du Pont de Nemours and Company Inc.: Corpus Christi, Texas.

iv. FMC Corporation: South Charleston, West Virginia.

v. Inland Chemical Corporation: Manati, Puerto Rico.

vi. Stauffer Chemical Company: Le Moyne, Alabama; Louisville, Kentucky; Niagara Falls, New York.

vii. Vulcan Materials Corporation: Geismar, Louisiana; Wichita, Kansas.

2. Pesticidal active ingredient use pattern. The primary pesticidal use of CCl_4 is as a component of mixtures applied as fumigants to control infestations of insects in 1) harvested grains throughout storage, transfer, milling, distribution, and processing phases, 2) stocks of seed grains, and 3) household and similar furnishings and fabrics which are based principally upon wool. The content of CCl_4 in most such mixtures ranges from about 22 percent to 94 percent. Carbon tetrachloride is a relatively inexpensive, non-flammable diluent for chemicals which are more highly active, but which embody serious fire and/or toxicity hazards. It can also enhance the penetration and diffusion of the gaseous mixture throughout the mass of material being fumigated (Ludvik, 1980a).

Information indicates that CCl_4 is included in fumigant mixtures principally as a flame retardant rather than for pesticidal purposes (Ludvik, 1980a). It is used in grain fumigation principally because it is non-flammable in any concentration in air, and serves to reduce fire hazards of other fumigants such as ethylene dichloride, ethylene dibromide and carbon disulfide (Pierpont, 1979; Metcalf, Flint and Metcalf, 1962).

In 1977-78, 19,593,000 pounds of carbon tetrachloride fumigant formulations were applied to grains stored off-farm, while 8,607,000 pounds (annual averages) were applied to grains stored on the farm (Development Planning and Research Associates, 1980).

Minor pesticidal uses of CCl_4 include spot fumigation of grain mill equipment to control red flour beetles, confused flour beetles, and other cereal pests; spot fumigation for bakery, brewery, nut processing, spice mill and feed mill equipment to control various insect infestations; fumigation of household contents such as clothes, furs, and carpets, to kill book lice, clothes moths, and carpet beetles; application as a rodenticide to kill gophers and moles. The registrations for household purposes cover use in commercial operations such as vault fumigation and fumigation in warehouses under cover. These formulations are neither intended nor registered for use by the individual homeowner.

3. Tolerances. No carbon tetrachloride residues were detected in grain fumigated with CCl_4-containing formulations in petitions submitted in 1956. The analytical method employed at that time for detection of CCl_4 had a sensitivity of 1 to 2 ppm and was based on colorimetric determination of residues by the Fujiwara reaction. It was therefore concluded from these 1956 studies that no CCl_4 residues were likely to result from fumigation of grain with CCl_4-containing pesticides. As a result, exemptions from tolerances were established in 40 CFR 180.1005 for use of CCl_4 after harvest on barley, corn, oats,

popcorn, rice, rye, sorghum (milo) and wheat. These exemptions apply to the CCl_4 active ingredient in all post-harvest fumigants containing CCl_4 when applied to whole grains.

No tolerance limits were set, nor was an exemption from the requirement of a tolerance level was granted for carbon tetrachloride residues in corn grits and cracked rice used in the production of malted beverages. Conditions for the safe use of CCl_4 on these grains were established in 21 CFR 193.230, which also set a limit of 125 ppm of inorganic bromides for brominated fumigants (methyl bromide and ethylene dibromide) used for the same purpose (21 CFR 193.230).

CCl_4-containing formulations may be used in or on grain-mill machinery, provided EPA-approved label directions are followed. However, these formulations are not used extensively because they can severely choke milling machinery, resulting in delays in start-up following treatment (USEPA, 1979b). There are no tolerances set on CCl_4 residues for this practice because no residues were expected due to the volatility of the compound.

Although carbon tetrachloride is currently exempted from the requirement of a tolerance for residues in certain grains (barley, rice, wheat, oats, sorghum, rye, corn and popcorn) more sensitive detection methods have recently shown residues in several types of food, including flour (Kozak, 1980; Bontoyon 1980). Sensitivity of modern analytical procedures now allows detection of CCl_4 residues as low as 1 ppb. Therefore, in the

event that the Agency does allow continued registration of CCl_4, tolerances will be required for all grainsfor which CCl_4 is registered for use, meat, poultry, eggs, and milk, in accordance with sections 406, 408 and 409 of the Federal Food, Drug and Cosmetic act as amended. A more detailed discussion of the Agency's discovery of CCl_4 in flour follows in II. B.

4. Pesticidal inert ingredient use pattern. This rebuttable presumption does not include products containing CCl_4 as an inert. Carbon tetrachloride is currently registered as an inert ingredient in fifteen products. The registered uses of these products include use as a ground spray or crop duster insecticide and fungicide, as a lawnweed killer, and for control of bacterial and fungal slimes in pulp and paper mills. Information available to EPA indicates that in thirteen of these formulations where the active ingredient is naled, CCl_4 is a contaminant and makes up 0.18 to 0.4 percent of the naled formulation (naled is currently in pre-RPAR review). In the two products where carbon tetrachloride is listed as being present in larger amounts (15 percent and 18.5 percent), it has been replaced by another chemical solvent.

C. Environmental Occurrence

1. Occurrence in water. Carbon tetrachloride has been found in concentrations of less than one part per billion (ppb) in many sample waters such as rain, surface water, potable water and in the sea. Low levels have also been detected in snow.

In the National Organic Reconnaissance Survey (NORS) study

of drinking water from 80 cities, carbon tetrachloride was found in 10 percent of the sampled drinking water supplies at levels less than 2 to 3 micrograms per liter (ug/1) (USEPA, 1979a.) In New Orleans, CCl_4 was found in both blood plasma and drinking water. However, of the raw water samples analyzed, CCl_4 was found in only four, with a maximum concentration of 4 ug/1. Confirmatory analyses performed by an alternate analytical technique resulted in a level of 2 ug/1.

In a more recent drinking water study, the National Organics Monitoring Survey (NOMS) sampled 113 public water systems and found carbon tetrachloride at very low concentrations, compared to chloroform and other organics (USEPA, 1977). Ten percent of the samples were positive for CCl_4, with mean values ranging from 2.4 to 6.4 ug/1.

2. Occurrence in air. Carbon tetrachloride has been measured extensively in the atmosphere and there is a good understanding of its distribution. It is primarily of anthropogenic origin (Altshuller, 1976; Lovelock et al., 1974; Wilkniss et al., 1973; Singh et al., 1976, all as cited in USEPA, 1977); however, it has been released for such an extended period of time that concentrations do not vary globally.

A number of researchers have measured the amounts of CCl_4 in the atmosphere. It is evident that there are no major gradients in the atmospheric distribution of CCl_4, as the concentrations are very similar in the continental and marine air masses (about .00078 to .00091 mg/m^3). Comparison of the

amounts of CCl_4 in the northern and southern hemispheres reveals a slightly lower concentration in the southern hemisphere (National Research Council, 1978); however, the gradient is decreasing. Some high CCl_4 concentrations have been reported in urban air, although they are generally close to the background level of .00078 to .00091 mg/m^3 found in the continental air mass.

The highest level ever reported over an extended period of time was 0.0091 mg/m^3, found in Tokyo between April, 1974 and April, 1975, however, this finding has not been confirmed (Ohta et al., 1976, cited in National Research Council, 1978). The maximum quantity measured in the atmosphere, 0.117 mg/m^3, was detected in 1975 in Bayonne, New Jersey (Lillian et al., 1975). The ubiquitous occurrence of CCl_4 in air could result in contamination of food items and thus be the actual source of observed carbon tetrachloride residues in food.

D. Metabolism

The following discussion is abstracted from CCl_4 criteria documents (NIOSH, 1975 and USEPA, 1979a) and some of their references.

Nielson found that absorption of CCl_4 by mammals occurs readily through lung tissue and more slowly through the gastrointestinal tract and skin (Nielson and Larson, 1965 as cited in USEPA, 1979). In their studies, the largest proportion of absorbed CCl_4 was excreted unchanged from the lungs; the remainder was metabolized and excreted in urine. McCollister et

al. (1951), as cited in NIOSH (1975), exposed two monkeys to radiolabeled CCl_4 by inhalation (46 ppm for 139 or 300 minutes) and found 50% of the CCl_4 exhaled unchanged and 5% as carbon dioxide. Traces of the label appeared in urine and feces, but not as CCl_4. Beamer et al. (1950, in NIOSH, 1975) administered radiolabeled CCl_4 to monkeys by dermal exposure to CCl_4-saturated atmosphere and reported 100 times more CCl_4 in exhaled air than in blood. Steward and Dodd (1964, in USEPA, 1979) demonstrated human dermal absorption by having three human subjects immerse one thumb in CCl_4 and measuring the CCl_4 exhaled after 10, 20, and 30 minutes of immersion. The range of CCl_4 concentrations at these times were 0.025-0.819 ug/l, 0.25-3.27 ug/l, and 0.69-5.23 ug/l, respectively. Five hours after immersion, CCl_4 was still detectable in the subjects' exhalations, indicating that the subject had retained a small amount of CCl_4. The distribution of CCl_4 in the organs varies with the route of administration, its concentration, and the duration of exposure.

The acute toxicity of CCl_4 to the liver is dependent on its metabolic breakdown (NIOSH, 1975). Metabolites reported and identified to date include chloroform, hexachloroethane, and carbon dioxide (Butler, 1961; Fowler, 1969; as cited in NIOSH, 1975). Studies have found radioactive labeled carbon tetrachloride in fatty acids, microsomal proteins, and lipids of the liver (Gordis, 1969, Rao and Recknagel, 1969: as cited in NIOSH, 1975). Metabolites may promote lipid peroxidation, which

can disrupt normal membrane structure and function (Klaassen and Plaa, 1969; Litterst et. al., 1973; as cited in NIOSH, 1975).

E. Pesticide Regulatory History

Date	Action or recommendation
6/8/56 -	Pesticide Petition #81 for exemption from tolerance requirements for use on wheat, barley, oats, rye, corn (including sweet and popcorn) and sorghum (milo) was received by FDA.
4/13/66 -	A joint USDA-HEW statement published in FEDERAL REGISTER recommended implementation of a plan included discontinuation by 12/31/67 of registrations involving residues on food or feed for which a tolerance or exemption was lacking. However, extensions were granted until December 31, 1970 if progress was being made to support the conclusion that the registration could be continued without undue hazard to the public health.
1/12/68 -	PR Notice 68-4 proposed extension of CCl_4 "no residue" and "zero tolerance" registrations beyond 12/31/67 for use on animals and animal premises.
2/1/68 -	PR Notice 68-6 proposed cancellation of registrations for CCl_4 products for beans (dry), peanuts, and peas (dry) due to absence of finite tolerances or exemptions and insufficient progress in investigation to warrant conclusion that registration may be continued without undue hazard to public

health.

4/24/68 - PR Notice 68-6 proposed extension of CCl_4 "no residue" and "zero tolerance" registrations beyond 12/31/67 for use on grain bins, granaries and mushroom houses until 1/1/69.

11/13/68 - PR Notice 68-18 proposed extension of CCl_4 "no residue" and "zero tolerance" registrations beyond 1/31/68 until 1/1/70 for uses on beef cattle, dairy cattle, goats, sheep, swine, corrals, dairy barns, grain bins, granaries, milk rooms, poultry houses and mushroom houses.

2/26/70 - PR Notice 70-3 proposed extension of registered "No Residue" uses of CCl_4 when listed as an active or inert ingredient in the formulation, on beef cattle, dairy cattle, goats, sheep, swine, corrals, dairy barns, milk rooms, poultry houses and mushroom houses.

3/12/71 - PR Notice 71-3 proposed cancellation of registrations of CCl_4 products bearing directions for use on beef cattle, dairy cattle, goats, sheep, swine, corrals, dairy barns, milk rooms, poultry houses and mushroom houses.

Since 1971 there have been no significant EPA regulatory actions. Actions taken by OSHA and NIOSH are discussed in II.B.2.

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SUMMARY OF EVIDENCE TO SUPPORT REBUTTABLE PRESUMPTION AGAINST REGISTRATION

A. Chronic Effects

1. Introduction. A rebuttable presumption shall arise if the ingredient(s), metabolite(s), or degradation product(s) of a pesticide meet or exceed any of the risk criteria established in 40 CFR 162.11(a)(3). Carbon tetrachloride (CCl_4) meets or exceeds the risk criteria for a rebuttable presumption because:

a. It has induced oncogenic effects in experimental mammalian species (rats, mice, and hamsters) after oral administration, and;

b. It has produced chronic or delayed toxic effects in test animals and in humans:

(1) Chronic CCl_4-induced cirrhosis of the liver has been observed in mice, hamsters, rats, and rabbits after oral, subcutaneous, or inhalation exposure. Chronic exposure of humans has resulted in severe liver damage (NIOSH, 1975).

(2) Chronic administration of CCl_4 to rats has resulted in toxic effects to the kidney; chronic exposure of humans has resulted in nephrosis and degenerative changes in the nephron (NIOSH, 1975).

Due to the large number of toxicology studies which have been conducted on CCl_4, and in order to minimize duplication of effort, the Agency utilized existing reviews (i.e., secondary sources) of toxicology studies on CCl_4. The following Tables

1 and 2 are summaries of toxicity data from these secondary sources:

TABLE 1--CARCINOGENESIS STUDIES ON CARBON TETRACHLORIDE

STUDY	ANIMAL		ROUTE OF ADMINISTRATION	RESPONSE		PRENEOPLASTIC OR NEOPLASTIC EFFECT
	STRAIN(S)	AGE		TREATED	CONTROL	
A. Mouse Studies						
Edwards, Heston and Dalton (1942)	C57 Leaden	2.5 to 3 months	By gavage in olive oil	Hepatoma 27 to 50%	Hepatoma 0-3%	Positive
Eschenbrenner and Miller (1943)	Strain A	2 1/2 to 3 months	"	Hepatoma increased with duration of treatment	1%	Positive
Andervont and Dunn (1955)	C_3H	3 to 6 months	"	Hepatoma transplantable		Positive
Eschenbrenner and Miller (1946)	Strain A	3 months	"	Hepatoma; No-dose-response	1%	Positive
NCI (1977)	$(B6C3)F_1$	35 days	"	98% to 100% liver carcinoma; 22-57% adrenal pheochromocytoma	1 to 11% 0%	Positive
Edwards (1941)	C_3H, Strain A	3-6 months 2-3 months	"	Hepatoma 88 to 100%	1 to 27%	Positive
Edwards and Dalton (1942)	C_3H, Strains A,C,Y	1-5 months	"	Hepatoma 88% in male	1 to 27%	Positive
Leduc and Wilson (1959)	EUB	—	"	Hepatoma transplantable	—	Positive
Confer and Stenger (1966)	C_3H	5 weeks	Intrarectal in olive oil	Hepatoma 88%	4%	Positive

TABLE 1-- CARCINOGENESIS STUDIES ON CARBON TETRACHLORIDE (CONT'D)

STUDY	ANIMAL STRAIN(S)	ANIMAL AGE	ROUTE OF ADMINISTRATION	RESPONSE TREATED	RESPONSE CONTROL	PRENEOPLASTIC OR NEOPLASTIC EFFECT
B. Rat Studies						
Rueber and Glover (1967)	Buffalo	4 weeks	S.C. injection of 50% CCl_4 in corn oil	Hyperplasia, hyperplastic nodules	0%	Positive
Rueber and Glover (1970)	Osborn-Mendel, Wistar, Japanese	12 weeks	S.C. injection of 50% CCl_4 in corn oil	Carcinomas, hyperplastic nodules, cirrhosis	--	
NCI (1977)	Osborn-Mendel	52 days old	By gavage in corn oil	Liver tumors and cirrhosis in both sexes	0 to 1% 0 to 2%	Positive
Cameron and Karunaratne	Albino	150 gm b.w.	SC injection of pure CCL_4	Cirrhosis and hyperplastic nodules	--	Positive
Costa et al. (1963)	Wistar Albino	--	Inhalation for 7 months	Hyperplastic liver nodules	--	Positive
C. Hamster Studies						
Della Porta et al. (1961)	Syrian Golden	12 weeks	By gavage in corn oil	Carcinoma of the liver	--	Positive
D. Dog Study						
Bollman and Man	--	--	--	Cirrhosis	--	Short term
Lawson and Wing	--	--	--	Cirrhosis	--	Short term

Carcinogen Assessment Group, Preliminary Evaluation of Carbon Tetrachloride, October 3, 1977

TABLE 2--A SUMMARY OF THE TOXIC EFFECTS OF CARBON TETRACHLORIDE (CLEMENT ASSOCIATES, INC.)

Route	Species	Dose and Duration	Effects	Reference
Oral	Dog	0.5 ml/kg, sacrifice after 48 hours	Fresh central liver necrosis	Gardner et al. 1924[1]
		0.05-0.25 ml/kg, sacrifice after 48 hours 0.01 ml/kg, sacrifice after 48 hours	Liver parenchymal cells swollen and pale No microscopic or gross changes observed	
	Rabbit	0.1-6.0 ml/kg (no details on time to sacrifice)	Centrilobular necrosis of liver	
	Monkey	1-2 ml/kg, 3 days a week for 176 days	Liver cell vacuolation and swelling, fat accumulation in liver lobules	
Subcutaneous	Rat	0.4 ml/kg, autopsies 2, 4, 8, 16, 20, 24, 30, 36, 42, 48, 72, 96, 120, and 168 hours after dose	Liver and kidney damage at 4 hours. Kidneys normal by 48 hours, livers normal by 120 hours	Lundh 1964[1/]
		4 ml/kg, autopsies same as above	Kidney damage at 2 hours, liver damage at 4 hours. Kidneys almost normal at 120 hours, liver still damaged	
		0.4 ml/kg, every 3 days over periods of 72 hours-12 weeks, autopsies at 72 hours and at 2, 3, 4, 5, 6, 7, 8, 10, and 12 weeks	At 2 weeks kidney changes persisted between injections, and at 2 weeks fibrotic and cirrhotic changes began.	

TABLE 2--A SUMMARY OF THE TOXIC EFFECTS OF CARBON TETRACHLORIDE (CONT'D.)

Route	Species	Dose and Duration	Effects	Reference
Subcutaneous	Rat 1969[2]	0.15 ml/100 g, twice a month for 5 months	No mortality in younger animals; liver showed fat accumulation, necrosis, more apparent in males than females	Chaturvedi
Intraperitoneal	Rat	0.125 mg/g, sacrifice at 4-120 hours	Liver damage maximum at 48 hours, normal at 120 hours; serum OCT maximum at 48 hours, still high at 96 hours; tissue OCT maximum at 48 hours, decreased, then increased significantly at 120 hours	Musser and Spooner 1968[1/]
Intraperitoneal	Guinea pig	5, 25, 50, 75, 150 mg/kg, sacrifice at 24 hours after hood sampling	Serum OCT values elevated, liver damage and lipid accumulation after all doses except 5 mg/kg	DiVincenzo and Krasavage 1974[1/]
Inhalation	Guinea pig	25-400 ppm, 8 hours/day, 200 days	High mortality, optic nerve and ocular muscle degeneration	Smyth and Smyth 1935 and Smyth et al. 1936
	Rat	50-400 ppm, 8 hours/day, 189 days	Cirrhosis of liver, microscopic nerve changes	
	Monkey	50-200 ppm, 8 hours/day, 225 days	Fatty infiltration of liver	
Inhalation	Rat	400 ppm, 0.05 hours daily, 94 days	No effect	Adams et al. 1952[1/]
		400 ppm, 1 hour daily, 46 days	Decreased growth rate, signs of liver cirrhosis	
		400 ppm, 1 hour daily for 173 days	Increased liver, kidney weight; increased clotting time; liver degeneration; slight tubular degeneration of the kidney	

TABLE 2--SUMMARY OF THE TOXIC EFFECTS OF CARBON TETRACHLORIDE (CONT'D)

Route	Species	Dose and Duration	Effects	Reference
		100 ppm, 0.3 hours daily for 94 days	No effect	Adams et al. 1952[1] (continued)
		200 ppm, 0.3 hours daily for 192 days	50% mortality, depression of growth in males	
Guinea pig		400 ppm, 7 hours daily, 5 days per week, for 4 weeks	14/16 died; increased liver, kidney weight; fatty degeneration and cirrhosis of liver; slight tubular degeneration	
		200 ppm as above	12/16 died, similar effects as above	
		100 ppm as above	11/16 died, similar effects as above	
		50 ppm as above	All survived, similar effects as above	
Inhalation	Rats, both sexes	19,000 ppm for 2.2 hours, 1,200 ppm for 4 hours, 7,300 ppm for 8 hours, 4,600 ppm for 8 hours, 3,600 ppm for 12 hours	Deaths due to respiratory failure; symptoms included stupor, uncoordination, unconsciousness, increase in clotting time; increase in liver lipid content	
		3,000 ppm for 0.1 hour	No effect	

TABLE 2--A SUMMARY OF THE TOXIC EFFECTS OF CARBON TETRACHLORIDE (CONT'D)

Route	Species	Dose and Duration	Effects	Reference
		800 ppm for 0.5 hour	No effect	Adams, et al. 1952[1/] (continued)
		50 ppm for 7.0 hours	No effect	
	Rabbit	100 ppm, 7 hours daily, 5 days per week, 30 weeks	Decreased growth, increased clotting time, liver cirrhosis	
		50 ppm as above	Similar effects to above	
		25 ppm as above	Increased liver weight, slight cirrhosis	
	Monkey	100 ppm, 7 hours daily, 5 days per week, 32 weeks	No effect on appearance, organ weights, and behavior; slight decrease in growth; slight increase in liver lipid content	
	Monkey	50 ppm as above	No effect	
Inhalation	Cats	10,000 ppm for 15 to 240 minutes	Increase in kidney, liver, adrenal gland weights; increase in liver and kidney lipid content; liver displayed central necrosis	Wong and DiStefano 1966[2/]
Inhalation	Rats	4.6 mg/liter	100% mortality in 8.0 hours	Prendergast et al. 1967[1/]
		15.6 mg/liter	100% mortality in 4.0 hours	
		119.7 mg/liter	100% mortality in 2.2 hours	

TABLE 2--A SUMMARY OF THE TOXIC EFFECTS OF CARBON TETRACHLORIDE (CONT'D)

Route	Species	Dose and Duration	Effects	Reference
		6.1 mg/m^3 for 90 days	No effect	Prendergast et al. 1967[17] (continued)
		61 mg/m^3 for 90 days	Decreased growth rate, liver degeneration and fibrosis	
Inhalation	Rats	515 mg/m^3, 8 hours daily, 5 days per week, for 6 weeks	Interstitial inflammation of lungs, fatty changes in liver	
	Guinea pig	515 mg/m^3 Same as above	3/15 died, inflammation of lungs, increased lipid content of liver, fibrosis of liver, signs of cirrhosis	
	Rabbit	515 mg/m^3 Same as above	Similar changes in lung and liver as above	
	Dogs	515 mg/m^3 Same as above	Loss of weight, changes in lung and liver	
		61 mg/m^3, continuously for 90 days	Loss of weight, moderate fatty degeneration of liver	
		6.1 mg/m^3, continuously for 90 days	No effect	

TABLE 2--A SUMMARY OF THE TOXIC EFFECTS OF CARBON TETRACHLORIDE (CONT'D)

Route	Species	Dose and Duration	Effects	Reference
	Monkeys	515 mg/m^3, 8 hours daily, 5 days per week, for 6 weeks	1/3 died, weight loss, fatty liver, lung inflamation	Prendergast et al. 1967[17] (continued)
		61 mg/m^3, continuously for 90 days	Decreased growth rate, enlarged fatty livers	
		6.1 mg/m^3, continuously for 90 days	No effect	

1/ As cited in NIOSH (1975)
2/ As cited in EPA (1979)

For each of the three RPAR risk criteria which have been met, only certain of these studies are discussed in the following pages.

2. Oncogenicity -- a. Animal studies. The following studies reviewed in USEPA (1977) and NIOSH (1975) collectively present evidence that CCl_4 is oncogenic in experimental mammalian species, and may be oncogenic in man.

(1) NCI Bioassay. The NCI Bioassay of Trichloroethylene, as cited in USEPA (1979a), also included testing of carbon tetrachloride. In this study CCl_4 was used as a positive control. The study used B6C3F1 mice, which were 35 days old at the beginning of the study. There were 50 animals in each experimental group, one group for each sex at dosage levels of 1,250 and 2,500 mg/kg/day. Doses were administered by oral gavage in a corn oil solution five times a week for 78 weeks; survivors were sacrificed after 92 weeks. There were 20 matched control mice of each sex that were given corn oil only. Treated groups were also compared to pooled controls from concurrent experiments. Complete histological examinations were performed on all mice, including those that died in the course of the experiment.

Most male and female mice treated with CCl_4 were dead by 78 weeks, as indicated in Table 3 as follows:

TABLE 3-- SURVIVAL OF MALE MICE TREATED WITH CARBON TETRACHLORIDE

Treatment Group	Initial	78 Weeks	91-92 Weeks
Controls			
Matched	20	13 (65%)	7 (35%)
Pooled	77	53 (69%)	38 (49%)
Low Dose	50	11 (22%)	0 (0%)
High Dose	50	2 (4%)	0 (0%)

Survival of Female Mice Treated with Carbon Tetrachloride

Treatment Group	Initial	78 Weeks	91-92 Weeks
Controls			
Matched	20	18 (90%)	17 (85%)
Pooled	80	71 (89%)	65 (81%)
Low Dose	50	10 (20%)	0 (0%)
High Dose	50	4 (8%)	1 (2%)

National Cancer Institute (1976)

Hepatocellular carcinomas were found in almost all mice receiving CCl_4, including those dying before termination of the test. The first carcinomas were observed in low dose females at 16 weeks, in high dose females at 19 weeks, in high dose males at 26 weeks, and in low dose males at 48 weeks, compared to 72 weeks for pooled control males and 90 weeks for pooled control females as indicated in Table 4 as follows:

TABLE 4--CARCINOMAS OF THE LIVER IN MICE TREATED WITH CARBON TETRACHLORIDE

Treatment Group	Males	Females
Controls		
Matched	2/19 (11%)	1/20 (5%)
Pooled	5/77 (6%)	1/80 (1%)
Low Dose	49/49 (100%)	40/40 (100%)
High Dose	47/48 (98%)	43/45 (96%)

National Cancer Institute (1976)

Thrombosis of the atrium of the heart was seen in 9 of 41 high dose female mice, or 22 percent, all of which died with carcinomas of the liver.

EPA summarized the results of this study by saying that it "found carbon tetrachloride to be highly carcinogenic for liver in mice" (USEPA 1979). Furthermore, in a preliminary evaluation of carbon tetrachloride, EPA noted that "because of the number of positive reports of CCl_4-induced hepatic tumors in mice and rats, the National Cancer Institute (NCI 1977) included CCl_4 in their bioassay program as a positive control for various halogenated hydrocarbons" (USEPA 1977).

(2) "Criteria document on carbon tetrachloride" (NIOSH, (1975). A number of cancer studies were summarized in this report.

(a) Studies were conducted by Edwards (1941), Edwards and Dalton (1942), and Edwards et al. (1942), as cited in NIOSH (1975), in which five strains of mice (C3H, A, Y, C, and L) were fed 0.1 ml of a 40 percent solution of carbon tetrachloride in olive oil by stomach tube 2 or 3 times a week. C3H and A strain mice received a total of 23-58 feedings and were autopsied 2-147 days after the last feeding. Hepatomas were found in 88 percent (126/143) of the C3H mice and in 100 percent (54/54) of the A strain mice, compared to normal incidences of 10 percent for C3H and 0.5 percent for A strain mice of comparable ages. Hepatoma incidences of 60 percent, 82 percent and 47 percent were found in Y, C, and L strain mice, respectively, compared to normal

incidences of 2 percent at comparable ages. Hepatic tumors usually occurred in multiples, as many as 10 per liver. No metastases, other liver tumors, or tumors at other sites were seen.

(b) Eschenbrenner and Miller (1946), as cited in NIOSH (1975), established that a single oral dose of 12.5 ul/kg or more of carbon tetrachloride caused liver cell necrosis in both male and female mice. Also, 4-month old A strain mice were administered 120 daily doses of 6.25, 12.5, 25, or 50 ul/kg of carbon tetrachloride dissolved in olive oil by stomach tube. When they were examined 1 month after the last dose, corresponding to a period of 5 months from the initiation of treatment, all of the mice that had received doses of 12.5 ul/kg or more had hepatomas, whereas no hepatomas were found in the mice given doses of 6.25 ul/kg. When other groups of mice were given 30 doses of 100, 50, or 25 ul/kg of carbon tetrachloride at 4-day intervals, microscopic hepatomas were found in 2 of 10 mice at the 25 ul/kg level; larger, macroscopic hepatomas were found in two-thirds of the mice given higher doses.

(c) Della Porta et al. (1961), as cited in NIOSH (1975), administered carbon tetrachloride by stomach tube as a 5 percent solution in corn oil to 10 male and 10 female 12-week-old Syrian golden hamsters once a week for 30 weeks. During the first 7 weeks, the carbon tetrachloride dose was 12.5 ul, which was reduced to 6.25 ul for the remaining 23 weeks, roughly corresponding to doses of 125 and 62.5 ul/kg for the animals that

weighed approximately 100 g. The animals were observed for an additional 25 weeks and all survivors were sacrificed on the 55th week after the first treatment. Only five males and three females survived to the end of the experiment; these and two females that died in the 43rd and 54th weeks all had one or more liver-cell carcinomas. All of the nine animals that died or were killed earlier during the dosing period showed changes consistent with postnecrotic cirrhosis.

(d) Johnstone (1948), Simler et al. (1964), and Tracey and Sherlock (1968), as cited in NIOSH (1975), have reported three case studies where hepatic cancer was found in humans after carbon tetrachloride poisoning, although a causal connection was not definite.

b. Preliminary risk assessment. After having reviewed a number of studies for its report "Ambient Water Quality Criteria--Carbon Tetrachloride" (USEPA 1979a), EPA concluded, "there is sufficient weight of evidence to conclude that CCl_4 is a carcinogen in laboratory animals and with appropriate assumptions is interpreted to be a suspect human carcinogen." The Carcinogen Assessment Group of EPA (USEPA, 1977) has also concluded that "there are multiple studies demonstrating significant increases in tumors of the liver in mice, rats and hamsters treated with carbon tetrachloride. Both sexes are responsive to the oncogenic effect of carbon tetrachloride in the liver."

40 CFR 162.11(a)(3)(ii)(A) states that an RPAR shall arise

if the pesticide induces oncogenic effects in experimental mammalian species or in man as a result of oral inhalation or dermal exposure. Based on the information in this Position Document the Agency concludes that the risk criteria for oncogenicity has been exceeded.

3. Other chronic effects - liver (hepatotoxicity) --

a. Animal studies. Chronic administration of CCl_4 to laboratory animals results in toxic injury to the liver. The most prominent effect is cirrhosis of the liver, which has been observed in mice, hamsters, rats, and rabbits, but not monkeys, after oral or inhalation administration.

The EPA Ambient Water Quality Criteria Document (USEPA 1979a) discusses studies concerned with the chronic effects of CCl_4. The following discussion is abstracted from that document:

Edwards and Dalton (1942), in a study of the oncogenic properties of CCl_4, gave A strain male mice 0.1 ml of a 40 percent CCl_4-olive oil solution by gastric tube 2 or 3 times a week. The mice, autopsied after 23 and 58 doses, showed liver cirrhosis coincidental with hepatomas. Also using oral administration, Della Porta et al. (1961) gave Syrian golden hamsters 0.25 ml of a 5 percent CCl_4-olive oil solution weekly for 7 weeks in a study of the hamsters' response to liver carcinogens. This dose was reduced to 0.125 ml and continued for 23 weeks. All of the animals dying during the administration period (10/20) had cirrhosis of the liver. Animals sacrificed

between 43 and 55 weeks showed cirrhotic changes coincident with liver tumors.

Three studies of the chronic effects of CCl_4 administered by inhalation are cited by NIOSH (1975). The following discussion is abstracted from that document:

In a series of experiments, Smyth and Smyth (1935) and Smyth et al. (1936) investigated the effect of chronic exposure of rats and monkeys to a range of CCl_4 concentrations for periods up to 45 weeks. The rats were exposed to 50, 100, 200, or 400 ppm for 8 hours a day, 4 to 6 times a week, for a total of 150 or 189 exposures (about 25 to 45 weeks). At the low concentrations, and with increasing severity at the high concentrations, they observed liver cirrhosis, among other toxic effects, in most animals. In the monkeys, which were exposed 8 hours a day, 4 to 6 times a week, over a period of 93, 275, or 321 days to either 50 or 200 ppm, the investigators reported no cirrhosis. Adams et al. (1952) administered CCl_4 by inhalation to rats, guinea pigs, rabbits, and monkeys. The standard exposure regime was 7 hours a day, 5 days a week, for a total of 150 to 200 exposures (30 to 40 weeks). Common effects observed were cirrhosis and fatty degeneration of the liver; their findings are reflected in Table 5 as follows:

TABLE 5 -- TOXIC EFFECTS OF CHRONIC CCl_4 INHALATION [1/]

Species	Number	Exposure Level (ppm)	Effects
Rats	30-49 at each level	5	No abnormal effects.
		10	Increased liver weight and fatty liver degeneration.
		25	As above.
		100	As above and cirrhosis.
		200	As above.
		400	As above.
Guinea Pigs	8-9 at each level	5	Increased liver weight.
		10	As above and fatty liver degeneration.
		25	As above and cirrhosis.
		100	As above.
		200	As above.
		400	As above.
Rabbits	2-4 at each level	25	Fatty liver degeneration and cirrhosis.
		50	As above, increase in kidney weight and blood clotting time.
		100	As above.
Monkeys	2 at each level	25	No abnormal level findings.
		50	Loss of body weight.
		100	Unspecified microscopic liver changes.

1/ Adams et al. (1952), as cited in NIOSH (1975)

b. Human studies. Toxic effects have been seen in the livers of humans chronically exposed to CCl_4. The following discussion is abstracted from EPA (1979a), which cites as its primary source a review by Von Oettingen (1964) of chronic CCl_4 poisonings.

> "After chronic CCl_4 exposure, the liver may be mottled in appearance and have signs of fat accumulation even in the absence of clinical symptoms of liver injury. More severe damage is manifested by centrilobular necrosis, hemorrhage, and collapse of the lobules with condensation of the reticular framework in these areas. In cases of prolonged exposure, some liver regeneration may occur."

The NIOSH Criteria Document (1975) cites a number of case histories and studies of the toxic effects of prolonged exposure to CCl_4. The most commonly reported effects include jaundice, hepatic necrosis, and cirrhosis. These studies are reflected in Table 6 as follows:

TABLE 6--CHRONIC TOXIC EFFECTS OF CARBON TETRACHLORIDE IN LIVER AND KIDNEY IN HUMANS

No. of Individuals	Duration and Level of Exposure	Effects	Other Factors	References[a/]
1	11 years	Jaundice	Also exposed to Other chemicals	Gray (1947)
2	4 years, 10-100 ppm	Liver necrosis		Dellian and Wittgens (1962)
1	"years"	Cirrhosis, hepatic cancer		Johnston (1948)
1	17 months	Jaundice, anuria, hepatic cancer		Tracey and Sherlock (1968)
27	N/R[b]	Kidney dys-function	Occupationally exposed	Barnes and Jones (1967)
51	28-43 days per year, 3-27 years	Liver dys-function	Occupationally exposed	Rabes (1972)
13	5 to 1,680 ppm	Indications of jaundice	Occupationally exposed	Smyth and Smyth (1935) and Smyth et al. (1936

a/ As cited in NIOSH (1975)
b/ Not reported

A concomitant factor in both fatalities and cases of severe liver damage due to CCl_4 exposure is often alcohol consumption (Gray, 1947; Tracey and Sherlock, 1968; Joron et al., 1957; New et al., 1962; and Thompson, 1955; all as cited in NIOSH 1975). Experimental studies in laboratory animals have shown that pretreatment with alcohol potentiates the hepatotoxic effect of CCl_4 (Traiger and Plaa, 1971; Wei et al., 1971; Cornish and Adefuin, 1966; all as cited in NIOSH 1975). However, reports of simultaneous exposure to CCl_4 of nondrinkers and occasional consumers of alcohol indicate that habitual alcohol consumption is not necessary to potentiate the effects of CCl_4 (Von Oettingen, 1964, as cited in USEPA 1979a).

c. RPAR conclusion. 40 CFR 162.11(a)(3)(ii)(B) states that an RPAR shall arise if the pesticide produces any other chronic or delayed effects in test animals at any dosage up to a level, as determined by the administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety.

Inhalation exposure to CCl_4 has resulted in increased liver weight and fatty liver degeneration in rats at 10 ppm, fatty liver degeneration and cirrohosis in rabbits at 25 ppm, and increased liver weight and fatty liver degeneration at 10 ppm in guinea pigs (Adams et al., 1952). Applicator exposure data available to the agency (Paulus et al., 1957) indicate that exposure levels for grain fumigators can far exceed the effect

levels observed in animals. Thus the Agency concludes that the risk criterion for chronic liver effects has been exceeded.

4. Other Chronic Effects - Kidney (Nephrotoxicity) --

a. Animal studies. Studies have shown that chronic administration of CCl_4 to laboratory animals results in toxic effects in the kidney. Smyth and Smyth (1935) and Smyth et al. (1936), as cited in NIOSH (1975), investigated the effect of chronic exposure of rats and monkeys to a range of CCl_4 concentrations for periods of up to 45 weeks. The rats were exposed to 50, 100, 200, or 400 ppm for 8 hours a day, 4 to 6 days a week for a total of 150 or 189 exposures (about 25 to 45 weeks). At low concentrations, and with increasing severity at high concentrations, they observed kidney damage in some animals, among other toxic effects. The monkeys, which were exposed to 50 or 200 ppm for 8 hours a day, 4 to 6 days a week, for 93, 275, or 321 days, showed no kidney damage.

b. Human studies. Toxic effects have been seen in the kidneys of humans chronically exposed to CCl_4. The following discussion is abstracted from EPA (1979a), which cites as its primary source a review by Von Oettingen (1964) of chronic CCl_4 poisonings:

> "After chronic CCl_4 exposure, toxic effects in the kidney include nephrosis due to distension of Bowman's capsule by albuminous precipitates and swelling of the lining cells. The convoluted tubules are swollen

and Henle's loop shows degenerative changes with the accumulation of granular, hyaline, and cellular casts in the tubules. Some cases display acute hemorrhagic nephritis. This is a morphologic description of the damage done to the kidney by the compound administered. These changes are not seen in the normal kidney."

The NIOSH Criteria Document (1975) cites a number of human case histories and studies of the toxic effects in the kidney, including necrosis and nephritis. The levels and duration of exposures varied from case to case. A summary of these studies is included in Table 6.

c. RPAR conclusion. 40 CFR 162.11(a)(3)(ii)(B) states that an RPAR shall arise if the pesticide produces any other chronic or delayed effects in test animals at any dosage up to a level, as determined by the administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety.

Inhalation exposure to CCl_4 has resulted in kidney damage to rats exposed to 50 ppm (Smyth and Smyth, 1935, and Smyth et al., 1936, as cited in N105H, 1975). Applicator exposure data available to the Agency (Paulus et al., 1957) indicate that exposure levels for grain fumigators can far exceed the effect levels observed in animals. Thus the Agency concludes that the risk criterion for chronic liver effects has been exceeded.

B. Human Exposure

1. Dietary exposure. The Agency has reviewed all available data on the exposure of humans to CCl_4 residues in food resulting from the pesticidal uses of CCl_4. Section "a" describes the CCl_4 residues remaining in flour and bread from application of CCl_4 formulations to wheat grain. Section "b" summarizes the residues in other foods. Section "c" estimates the human dietary burden which may result from the pesticidal use of CCl_4.

a. Carbon tetrachloride in wheat, flour and bread. The major pesticidal use of CCl_4 is as a fumigant-ingredient (often formulated with CS_2, EDB, and/or EDC) used postharvest on grains to arrest and prevent infestation. CCl_4 formulations are applied directly to grains in storage bins, silos, elevators, trucks and railcars. After application, the CCl_4 penetrates the grain in a time-dependent manner, binding to the bran, inner starch, and endosperm moieties of the grain. This binding is likely to give rise to the persistent CCl_4 residues in wheat flour and bread documented below.

A review of the literature indicates three studies of CCl_4 formulations applied to wheat [Wit (1969), Berck (1974), and Jagielski (1978)]. These laboratory studies present CCl_4 dose, storage, and residue loss conditions comparable to those in commerce.

(1) The Wit Study (1969). It was found that CCl_4 residues in flour range from 2.8 ppm to 11 ppm with levels of

CCl_4 in bread up to 70 ppb. The average retention of CCl_4 residues in bread was 0.27 percent of the levels in flour.

(2) The Berck Study (1974) . It was found that CCl_4 residues in flour ranged from 0.2 to 0.93 ppm, while residues in bran were higher (0.43 to 3.53 ppm). Bread baked from the flour had CCl_4 residues as high as 40 ppb, with an average retention of 7 percent of the flour levels (range 0.1 - 15 percent).

(3) The Jagielski Study (1978). It was found that flour had 0.6 to 1.6 ppm CCl_4 residues, while bran had 2.9 to 5.3 ppm CCl_4 residues. Bread baked from the flour had CCl_4 residues as high as 60 ppb, with an average retention of 0.4 percent of the flour levels.

These three studies are each generally comparable to commercial fumigation and aeration conditions. Each study was performed under laboratory conditions. The Agency infers that only an approximation to the actual retention behavior of CCl_4 residues in commercial flour and bread may be made from these studies. When considered together, the studies indicate that CCl_4 residues will probably occur in commercial flour from 0.2 to 2.8 ppm, in bran from 0.43 - 5.3 ppm, and in bread from 40 - 70 ppb, with a range of retention in bread of 0.3 - 7 percent of the CCl_4 residue levels in flour.

Recently, the Agency's Pesticide Laboratory in Beltsville, Maryland, in cooperation with the USDA, made preliminary determinations of CCl_4 residues in flour sampled from 11 U.S. cities and destined for the School Lunch Program (Bonotoyan,

1980). It was found that all flour samples analyzed (21) were positive for CCl_4, with a range of values of 5 - 261 ppb and an average of 51 ppb (S_x = 80 ppb). If the range of retention in the above studies (0.3 - 7 percent) is assumed to be accurate, then the calculated levels of CCl_4 residues in bread would be in the range of 0.02 - 18 ppb. The calculated upper limit of CCl_4 residues (18 ppb) is somewhat lower than the upper limit obtained from the Wit, Berck, and Jagielski studies (70 ppb).

b. Carbon tetrachloride residues in foods. At present, no data on CCl_4 residues in commercial food are available from the U.S. A British study made measurements of CCl_4 residues in food as part of a larger study investigating the impact of chlorinated hydrocarbons on the environment (McConnell, et al., 1975). The results of tests on wheat bread, beef, olive and cod liver oil, potatoes, apples and pears are presented in Table 7 along with expected daily intakes of CCl_4 residues from each food source as follows:

TABLE 7 -- CARBON TETRACHLORIDE RESIDUES IN FOOD 1/

FOOD	RESIDUES (ppb)	FOOD FACTOR PERCENTAGE	DAILY DIETARY INTAKE ng/day/person
WHEAT PRODUCTS:			
bread	5	10.36	777.00
MEAT:			
beef	7	10.81	1135.00
OILS:			
olive oil	18	0.038	8.10
cod liver oil	16	0.037	7.20
FRUITS and VEGETABLES:			
potatoes	8	5.43	651.59
apples	5	2.53	189.75
pears	4	0.26	15.60

1/ CCl_4 residue occurrence in listed foods taken from McConnell, et al., (1975). The daily dietary intake was calculated by multiplying the CCl_4 residue level times the food factor times 1500 g. total food ingested/day times 10^9 ng/g. The unit of daily dietary intake is, therefore, ng/day/person.

The McConnell study bears relationship to the U.S. dietary intake of CCl_4 residues insofar as the registered uses of CCl_4 in Britain are similar to those employed in the U.S. It is conceivable that some of the residues come from nonpesticidal uses of CCl_4, since the source of the CCl_4 residues in some of the foods in the study could not be determined. The Agency is not sure how closely the use patterns coincide between the United States and Great Britain. However, since there are no U.S. studies available to the Agency, the McConnell study will be utilized as a general indicator for occurrence of CCl_4 residues in food in the United States. Registrants are encouraged to submit residue data which document the amount of CCl_4 residues in each food reviewed above and identify the source of these residues.

(1) Food residues probably resulting from pesticidal uses of CCl_4 -- (a) Wheat and bread. Commercial wheat bread was found to contain an average of 5 ppb CCl_4 residues, which is likely to be the result of pesticide uses of CCl_4, in so far as CCl_4 formulations are repeatedly applied to wheat when necessary. Additionally, the Wit, Berck and Jagielski laboratory studies all demonstrated the persistence of CCl_4 residues in wheat grain, flour, and wheat bread.

If an average individual eats bread containing 5 ppb CCl_4 residues, then this individual would consume 777 ng of CCl_4/day. The commercial level of 5 ppb of CCl_4 in bread is compared to the laboratory level of 40 - 70 ppb, and the calculated bread level from the Agency flour studies of 0.02 - 18 ppb. It is notable that the 5 ppb level found in England falls into the range of CCl_4 calculated by the Agency in bread from U.S. flour. This suggests the validity of using the English study in estimating CCl_4 residues in the U.S.

While the grain discussed in the studies cited is wheat, it should be noted that CCl_4 is exempt from the requirement of a tolerance on barley, corn, oats, rice, rye, sorghum (milo) and popcorn as well. Although there are apparently no data on residues in these otther grains, if residues occur in wheat and wheat bread, they may also be expected in the other grains.

(b) Meat. The McConnell survey showed 7 ppb of CCl_4 in meat. If this is considered an average level of contamination, then daily ingestion would be 1135 ng of CCl_4/day/person. The presence of CCl_4 residues in meat is possible via the use of CCl_4 on cattle feed grains such as corn. The Agency identifies the actual level of CCl_4 residues in livestock diets and lack of an appropriate CCl_4 feeding study as data gaps.

(c) Milk, cheese, butter and eggs. The McConnell survey showed residues of CCl_4 in these foods. However, on July 1, 1980 EPA officials, in a telephone conversation with the British author, discovered that these residues were a combination of CCl_4 and 1,1,1-trichloroethane (Otakie, 1980). Accordingly, these residues have not been included in estimating the dietary burden of CCl_4. Nevertheless, the detection of CCl_4 in meat and the combined residues in dairy products suggests CCl_4 residues may be present in dairy products.

(2) Food residues resulting from unknown sources of CCl_4 --(a) Oils. It is difficult to explain CCl_4 residues in olive oil insofar as this oil is imported to this country and the source of CCl_4 residues is unknown.

(b) Fruits and vegetables. The contribution to the human diet of CCl_4 residues from fruits and vegetables is 1016 ng/day/person. The source of CCl_4 residues in potatoes, apples and pears is unknown; there are no U.S. registered pesticide uses for CCl_4 formulations on these crops.

c. Total dietary exposure to carbon tetrachloride. The total human dietary burden for all CCl_4 residues is the sum of the residues in or on all foods. Assuming that the occurrence of CCl_4 in the British study is representative of CCl_4 pesticidal residues in the U.S., the dietary intake of CCl_4 from all of the above foods is 2784 ng/person/day. From this estimated dietary intake, the total dietary burden (DB) from all sources of CCl_4 for a U.S. citizen weighing 60 kg is 4.64×10^{-5} mg/kg/day. Limiting the foods to those likely to be contaminated by the pesticidal use of CCl_4 (i.e., wheat and meat), the daily dietary intake of CCl_4 is 1912 ng/day/person and the corresponding dietary burden is 3.19×10^{-5} mg/kg/day.

2. Non-dietary exposure analysis. Non-dietary exposure to carbon tetrachloride includes applicators, persons in the vicinity of the application site, and workers who handle fumigated grain. CCl_4 is used to fumigate stored grain in farm storage facilities ("on-farm" and "off-farm" small scale), flat storage bins, bags, packaging and processing plants, and country elevators. Large facilities generally use aluminum phosphide, but CCl_4 is used more often at smaller facilitites.

a. Applicator exposure. Carbon tetrachloride is applied

for grain fumigation primarily by the "gravity distribution" method, by either surface application or layering. This method is practiced both on-farm and off-farm. Pesticide labels recommend that respirators be used in all applications, however, CCl_4 is apparently applied by many farmers using no protective measures. In general, full-face masks are not used (NIOSH, 1975). Fumigation is usually performed by two or more persons. A second method of CCl_4 application is "outside of car" application. In this usage, fumigation of grain stored in railway cars is accomplished by personnel standing outside the cars. CCl_4 is either poured from one or five gallon containers through vents located in the roof of the car, or sprayed into the car with a power sprayer.

Per 29 CFR 1910.1000, the OSHA standard for CCl_4 in air is as follows:

(1) 8 hr. time weighted average of 10 ppm - an acceptable 8 hr. ceiling concentration of 25 ppm.

(2) an acceptable maximum peak of 200 ppm for 5 minutes in any 4 hour period, above the acceptable ceiling concentration for an 8-hour shift.

Additionally, NIOSH (1975) has recommended that OSHA lower its limit to 2 ppm as a one hour ceiling.

The OSHA standard was promulgated with the intent of protecting employees who might be exposed to CCl_4 in their workplace. While the standard is aimed primarily at employees in pesticide manufacturing and formulating plants, it is unclear

whether it covers grain elevator workers, applicators, farmers or other persons who are exposed during and after grain fumigation.

Under FIFRA, the EPA has a responsibility to prevent unreasonable adverse effects to persons exposed to CCl_4 as a result of grain fumigation. The Agency is concerned that the no observable effect levels for chronic effects of CCl_4 closely approach the exposure levels deemed acceptable by the OSHA standard. EPA is also concerned that the high levels of exposure to CCl_4 measured during grain fumigation exceeds the OSHA standard and the NOEL's for chronic effects.

One study (Paulus et al., 1957 cited in NIOSH, 1975) provides the only data for CCl_4 exposure to applicators. In this study a mixture of 80 percent carbon tetrachloride and 20 percent carbon disulfide was applied and air samples were taken. Three separate groups of workers were involved, the first of which consisted of the applicators who sprayed the fumigant. These men generally wore respirators. The second group represented the personnel who tended the pump and barrels. The third group consisted of individuals who inspected the grain and corn after the fumigation process was completed. Members of these latter two groups did not usually wear respirator protection.

Results of analysis of simultaneous samples indicated that a ratio of CCl_4 to CS_2 vapors averaged 2.5 during the fumigation process. All of the reported CCl_4 air concentrations

were calculated by use of this ratio, and were not in fact actual measurements of CCl_4. The air samples were taken during fumigation in cylindrical bins, quonset huts, and other storage buildings. Out of a total of 36 measurements from 6 sites, fourteen ranged from 0 to 1,500 ppm CCl_4, eight from 1,501 to 4,500 ppm, nine from 4,501 to 15,000 ppm and five exceeded 15,000 ppm. The latter five values, found during fumigation of 18 foot cylindrical bins, exceeded 6,000 ppm of CS_2, for a total vapor concentration of over 20,000 ppm for CS_2 and CCl_4, which exceeds the 2 percent safe limit for the respirator canister. The reason for these high exposures is that the heavy fumigant vapors rolled down the inside of the bin and collected at the bottom where the fumigators stood.

Paulus also reported air concentrations in the work area occupied by the fumigatio crew members. Breathing zone samples for these workers, whose responsibilities included tending the pumps, opening barrels, metering the fumigant, and related duties, ranged from 0 to 7,700 ppm of CS_2 and 0 to 19,000 ppm of CCl_4. Due to the nature of the work these men performed, great variations in both concentration and duration of exposure were experienced. The values of these ranges were arrived at by calculation of weighted exposures. Test measurements on breathing zone samples indicated that the OSHA ceiling limit of 25 ppm for CCl_4 was exceeded at many locations for this group.

The third group of samples was taken after fumigation in order to determine potential exposure of grain inspectors.

Concentrations of CCl_4 near or above the OSHA ceiling concentration value of 25 ppm were found after seven days. CCl_4 residues in air samples from bins were measured at 80 to 135 ppm after two days, 16 to 60 ppm after seven days, and 16 to 19 ppm after fifteen days. This wide range of concentrations of CCl_4 vapors in the different bins probably resulted from the bins having different degrees of air tightness.

Exposure to CCl_4 by dermal contact can also occur in the work environment. Absorption of liquid CCl_4 through the skin has been shown to occur in humans and animals (Stewart et al., 1964, as cited in NIOSH, 1975); however, the results of this study were not conclusive.

No data are available on the potential for dermal and inhalation exposure of workers in sites not directly related to the site of fumigation (e.g. warehouse employees, ship loading crews etc.). However, exposure of such workers to CCl_4 could reasonably be expected due to CCl_4 residues remaining in fumigated grain over extended periods of time.

CCl_4 has a long life in the body (Neilson and Larson, 1965) and is readily absorbed through the lungs. No information is available for quantitively estimating the amount of CCl_4 that would penetrate the lungs.

Because of the lack of sufficient information, inhalation and dermal exposure estimates could not be developed.

OTHER RELEVANT ADVERSE EFFECTS

A. Teratogenicity

There is little information on the teratogenicity of carbon tetrachloride. EPA, in its Ambient Water Quality Criteria Document (USEPA 1979), summarized two studies:

1. Data concerning the teratogenicity of CCl_4 are scarce. Schwetz, et al. (1974) administered CCl_4 to Sprague-Dawley rats at 300 or 1,000 mg/l for 7 hours per day on days 6-15 of gestation. Results indicated that CCl_4 was not highly embryotoxic but that it does cause some degree of retarded fetal development such as delayed ossification of sternebra. A greater degree of maternal toxicity was found.
2. Bhattacharryya (1965) studied fetal and neonatal responses to hepatotoxic agents. He found that subcutaneous and intra-amniotic injections into fetuses only occasionally give rise to changes in the fetal liver. When changes do occur, they vary from sinusoidal dilation and congestion or well-marked variability of staining of liver lobules to occasional centrilobular or, rarely, massive necrosis.

The authors of this document stated that the teratogenic effects of carbon tetrachloride have not been conclusively demonstrated. However, Schwetz's study showed a statistically significant dose response in fetal weight and crown-rump length. Therefore, the Agency will further examine the possibility of fetotoxic effects.

Additional information is given in a report by the National Research Council (NRC, 1978) in which it was stated:

Smyth and Smyth (1935) and Smyth et al. (1936) observed the effects of chronic exposure to 50, 100, 200 or 1,000 ppm carbon tetrachloride in three generations of rats. No report of incidence of embryonic or fetal anomalies was made.

The Agency concludes that a data gap exists for teratogenic effects and certain studies may be required if CCl_4 is to remain registered. The Agency is currently seeking more information on these issues. If, upon further evaluation of all the toxicity and exposure data, the Agency determines that other such adverse effects are produced by exposure to carbon tetrachloride at any level up to a level exceeding possible human exposure (taking into account ample margins of safety), then the Agency will issue a supplemental notice or notices of rebuttable presumption against registration (RPAR) (s).

B. Mutagenicity

The mutagenicity or non-mutagenicity of carbon tetrachloride was not adequately demonstrated in the studies reviewed. However, the Agency has not thoroughly examined the mutagenic hazards of CCl_4, and will review and evaluate more recent studies. The issue will then be addressed either in a supplemental RPAR or in PD 2/3.

The EPA Ambient Water Quality Criteria Document (USEPA 1979a) reported that carbon tetrachloride was not found to be mutagenic in the Salmonella typhimurium or Escherichia coli reversion

tests (Kraemar et al., 1974). However, the authors of these studies noted that halogenated hydrocarbons are usually negative in the Ames test.

Indications of mutagenicity are given in a report by the National Research Council of the National Academy of Sciences (NRC 1978) in which it was stated:

> Barthelmess (1970) in his survey of mutagenic agents listed carbon tetrachloride as a chromosome-breaking agent. The National Science Foundation Panel on Manufactured Organic Chemicals in the Environment (1975) has reported some positive indications of the mutagenicity of carbon tetrachloride.

The lack of information on the mutagenicity of CCl_4 constitutes a data gap which must be filled if CCl_4 is to remain registered. The Agency is currently seeking more information on these issues. If, upon further evaluation of all the toxicity and exposure data, the Agency determines that other such adverse effects are produced by exposure to carbon tetrachloride at any level up to a level exceeding possible human exposure (taking into account ample margins of safety), then the Agency will issue a supplemental notice or notices of rebuttable presumption against registration (RPAR) (s).

C. Acute Toxicity (Animal Studies)

Numerous studies have investigated the effects of acute administration of carbon tetrachloride on several mammalian

species. The following Table 8 reflects the effects observed after exposure by ingestion, inhalation, absorption through skin, intraperitoneal injection, intravenous injection, and subcutaneous injection:

TABLE 8--ACUTE TOXIC EFFECTS OF CARBON TETRACHLORIDE

Route	Species, Age (Weight), Sex	Dose	Effects	Reference
Oral	Rats, 3 weeks, both sexes	2 ml/kg	50% mortality in 48 hours; increase in liver weight, fat, protein, and moisture, liver cells swollen with fat inclusions	Friedman et al. 1970
		6 ml/kg	100% mortality in 48 hours	
Oral	Rats, male		LD16 = 3,700 mg/kg LD50 = 6,000 mg/kg LD84 = 9,000 mg/kg	Kutepov 1968
	Rats, female		LD50 = 5,630 mg/kg	
	Mice, male		LD16 = 6,200 mg/kg LD50 = 9,100 mg/kg LD84 = 12,800 mg/kg	
	Guinea pigs, both sexes		LD50 = 5,700 mg/kg	
	Rabbits, male		LD50 = 5,760 mg/kg	
Oral	Rats, 350 g, male	2 ml/kg	Brief increase in hepatic blood flow and O_2 consumption, followed by decrease	Nakata and Higaki 1969

TABLE 8--ACUTE TOXIC EFFECTS OF CARBON TETRACHLORIDE (CONT'D)

Route	Species, Age (Weight), Sex	Dose	Effects	Reference
Oral	Dogs	50 ml (weight not specified)	Vomiting and diarrhea within 24 hours	Barsoum and Saad 1934
	Dogs		MLD (24 hours) = 4 g/kg; liver degeneration	
Inhalation	Rats, both sexes	4.6 mg/liter	100% mortality in 4.0 hours	Prendergast et al. 1967
		15.6 mg/liter	100% mortality in 2.2 hours	
		6.1 mg/m^3 for 90 days	No effect	
		61 mg/m^3 for 90 days	Decreased growth rate, liver degeneration and fibrosis	
Inhalation	Cats, 3-4 kg, both sexes	10,000 ppm for 15 to 240 minutes	Increase in kidney, liver, adrenal gland weights; increase in liver and kidney lipid content; liver displayed central necrosis	Wong and DiStefano 1966

TABLE 8--ACUTE TOXIC EFFECTS OF CARBON TETRACHLORIDE (CONT'D)

Route	Species, Age (Weight), Sex	Dose	Effects	Reference
Inhalation	Rats, both sexes	19,000 ppm for 2.2 hours, 1,200 ppm for 4 hours, 7,300 ppm for 8 hours, 4,600 ppm for 8 hours, 3,600 ppm for 12 hours	Deaths due to respiratory failure; symptoms included stupor, uncoordination, unconsciousness; increase in clotting time; increase in liver lipid content	Adams et al. 1952
		3,000 ppm for 0.1 hour	No effect	
		800 ppm for 0.5 hour	No effect	
		50 ppm for 7.0 hours	No effect	
Dermal	Guinea pigs, 400-900 g, male		LD50 = 9.4 ml/kg	Rowlabush et all. 1965
		0.5 ml	Irritation score = 4.1 (intact skin), 2.2 (abraded skin)	
	Rabbits, 1-4 kg, both sexes	0.5 ml	LD50 = 9.4 ml/kg Irrigation score = 2.8 (Intact skin), 4.0 (abraded skin)	

TABLE 8--ACUTE TOXIC EFFECTS OF CARBON TETRACHLORIDE (CONT'D)

Route	Species, Age (Weight), Sex	Dose	Effects	Reference
Dermal	Sheep, 35-45 kg	50 ml	3/5 died within 48 hours; 2/5 had kidney and liver dysfunction, liver recovered after 14 days	Setchell 1959
Intraperitoneal	Mice		24-hour LD50 = 2.6 mg/kg; ED50 for serum glutamic-pyruvic transaminase (SGPT) = 0.0085 mg/kg	Klaassen and Plaa
Intraperitoneal	Mice, 18-30 g, male	1-4 mg/kg	No significant increase in urine protein or glucose, swelling and necrosis in renal convoluted tubules	Plaa and Larsen 1965
		10 mg/kg	Liver impairment as shown by increase in pentobarbital sleeping time	
Intraperitoneal	Rats, male		24-hour LD50 = 1.9 ml/kg	Klaassen and Plaa 1967
Intraperitoneal	Rats, 4 weeks	2 ml/kg	11/24 mortality within 24 hours; survivors had increased liver weight, fat, and protein	Friedman et al. 1970

TABLE 8--ACUTE TOXIC EFFECTS OF CARBON TETRACHLORIDE (CONT'D)

Route	Species, Age (Weight), Sex	Dose	Effects	Reference
Intraperitoneal	Dogs, both sexes		24-hour LD50 = 1.5 ml/kg; ED50 for SGPT = 0.02 ml/kg; livers showed fat vacuolization and necrosis	Klaassen and Plaa 1967
Intravenous	Dogs		30 minute MLD = 90 mg/kg in ether-anesthetized animals; respiratory arrest preceded cardiac failure	Barsoum and Saad 1934
Subcutaneous	Mice, 18-25 g, male		10-day LD50 = 15 mg/kg; ED50 for increase in pentobarbital sleeping time (an indicator of liver impairment) = 0.033 mg/kg; livers showed central necrosis	Casals and Olitsky 1946
Subcutaneous	Mice, 3 months, both sexes		72-hour LD10 = 7.99 ml/kg; LD50 = 22.79 ml/kg; LD95 = 74.06 ml/kg; symptoms were drowsiness, unconsciousness, and lung congestion	Farag et al. 1966
Subcutaneous	Rats, 1-6 months, both sexes	0.15 ml/100 g	No mortality in younger animals, livers showed fat accumulation, necrosis, more apparent in males than females	Chaturvedi 1969

TABLE 8--ACUTE TOXIC EFFECTS OF CARBON TETRACHLORIDE(CONT'D)

Route	Species, Age (Weight), Sex	Dose	Effects	Reference
Subcutaneous	Rabbits	1.0 and 2.0 g/kg	No mortality in 7 days	Barsoum and Saad
		3.0 g/kg	All died in 7 days	
		4.0 g/kg	All died in 4 days	
Subcutaneous	Pigs, 25-66 days	0.6 ml/kg	No symptoms, no gross liver changes, microscopic necrosis in each liver lobule	White 1939
		1.0 ml/kg	Lethal in 12 hours	

Clement Associates, Inc., 1980b.

In addition to observing acute effects, a few studies have investigated the relationship between carbon tetrachloride's hepatotoxicity and nephrotoxicity. Wong and DiStefano (1966) measured the increase in lipid content of the liver, kidney, and adrenal gland of cats exposed once by inhalation. Because of a difference in the rate of fat accumulation in the liver and kidney, the authors concluded that injuries to these organs are independent of each other. In another study, Setchell (1959, as cited by Clement, 1980b) observed that in carbon tetrachloride poisoning in sheep, death always occurred in conjunction with kidney failure, but not with liver dysfunction. His conclusion was that severe liver dysfunction with moderate kidney impairment is insufficient to cause death.

Studies have also investigated the potentiation of the toxic effect of carbon tetrachloride by ethanol. Wei et al. (1971b) pretreated rats with a subcutaneous injection of ethanol (4 g/kg) 18 hours before an injection of carbon tetrachloride (0.25 ml/kg, 1:4 by volume with corn oil). The treated animals showed an increase in serum glutamic-pyruvic transaminase (SGPT) activity, (an indicator of liver cellular damage) over the animals receiving glucose, ethanol, or carbon tetrachloride alone, but no change in liver triglyceride (and thus no basic change in lipid metabolism). It should be noted that the route of application of both ethanol and CCl_4 in this study are not what would be experienced by humans. A similar effect on SGPT activity was found in dogs (Klaassen and Plaa 1967).

From the studies cited it is reasonable to conclude that acute exposures to carbon tetrachloride have hepatotoxic effects including cell necrosis and lipid accumulation (e.g., Friedman et al. 1970, as cited by Clement, 1980b, Wong and DiStefano, 1966, Klaassen and Plaa, 1967) and, to a lesser extent, nephrotoxic effects (Setchell, 1959, Plaa and Larson, 1965, cited by Clement, 1980b). The cause of death depends on tne route of exposure: kidney and/or liver failure results from oral exposure (Friedman et al., 1970; Kutepov, 1968, as cited by Clement, 1980b); depression of the central nervous system and respiratory failure from inhalation (Nakata and Higaki, 1969; Adams et al., 1952, as cited by Clement, 1980b); and lung congestion and central nervous system depression from injections (Farage et al., 1966, as cited by Clement, 1980b). No-effect levels were not investigated thoroughly, but were reported for inhalation by rats to range from 18,876 mg/m^3 for 0.01 hours (Adams et al., 1952) to 6.1 mg/m^3 for 90 days (Prendergast et al., 1967).

D. Human Case Histories and Epidemiologic Studies

The toxic effects of CCl_4 have been studied in humans as a result of accidental or intentional poisoning. Human data are available in case history studies or retrospective epidemiologic studies of occupational exposures. Acute symptoms include headache, nausea, vomiting, weakness, blurred vision, optic damage, and liver and kidney dysfunction. Fatalities are attributed to renal failure and hepatic necrosis and often occur in conjunc-

tion with a history of alcohol consumption or exposure to other chemicals. The studies are reflected in Table 9 as follows:

TABLE 9--SUMMARY OF EPIDEMIOLOGIC STUDIES

Route of Exposure	Level of Exposure	Number of Subjects	Type of Operation	Observations	Reference[1/]
Inhalation	10-80 ppm	"several"	Drycleaning	Nausea, dizziness, vomiting, headache	Elkins 1942
N/R[2/]	40-375 ppm	9	Multigraph printing	Nausea, loss of appetite, weight	Elkins 1942
N/R	5-1,680 ppm	77	Carbon tetrachloride manufacture, dry cleaning, others	35/77 had restricted visual fields; 13/67 had evidence of jaundice; hematology and kidney function tests showed no effect	Smyth et al. 1936 and Smyth and Smyth 1935
N/R	7.7 years average 6.4-9.5 ppm	62 workers	Cleaning	Reduced visual fields, corneal sensitivity	Moeller 1973
N/R	45-97 ppm	17	Cleaning	Nausea, loss of appetite, headache; no abnormal visual fields, SGOT levels	Kazantzis and Bomford 1960
N/R	N/R	27	Fluorocarbon	Kidney dysfunction compared to control group	Barnes and Jones 1967
N/R	N/R	675	Cleaning	Nausea, headaches weakness, abdominal cramps	Doyle and Baker 1944

Table 9--SUMMARY OF EPIDEMIOLOGIC STUDIES (CONT'D)

Route of Exposure	Level of Exposure	Number of Subjects	Type of Operation	Observations	Reference[1/]
N/R	28-43 per year for 2-27 years	51 workers 27 controls	Cleaning	Indications of liver dysfunction	Rabes 1972

1/ As cited in NIOSH (1975)
2/ Not reported

Source: Clement Associates, Inc., 1980a.

REQUEST FOR INFORMATION

A. Dietary Exposure

The Agency requests all available data on residues of CCl_4 in feed and food (particularly bread, meat, milk and eggs). The Agency does not have any data from a feeding study of grain treated with CCl_4 and any resulting residues in meat, milk and eggs, and solicits information regarding these potential residues.

B. Applicator Exposure

To accurately determine inhalation exposure, new data on the concentrations of carbon tetrachloride in the air during the entire fumigation process should be obtained.

Hands are likely to receive the greatest dermal exposure during mixing, loading and application. Data should be developed estimating potential exposures from accidental spills, including frequency, duration, and quantity resulting from these spills.

The lung and dermal penetration rate and data on the extent of human dermal contact with carbon tetrachloride should be obtained through toxicological studies on animals.

C. Teratogenicity, Mutagenicity and Reproductive Effects

The Agency requests that all available data on teratogenicity and mutagenicity be submitted, and also solicits information on reproductive effects, especially on spermatogenesis.

D. Non Grain Fumigant Uses

The Agency requests information on the extent of use and exposure to applicators from the minor pesticidal uses of CCl_4 discussed in I.B.2.

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All written comments and information filed pursuant to this notice will be available for public inspection in the office of the Chemical Information Division Document Control Officer, Office of Pesticides and Toxic Substances (TS-793), EPA, Rm. E-447, 401 M St. SW, Washington, D.C. 20460 from 8:30 a.m. to 4 p.m. during normal working days. Interested persons are encouraged to take advantage of the opportunity to inspect Agency files during normal working hours. All of the information received may serve as a basis for final determination pursuant to 40 CFR 162.11(a)(5). The Agency does not plan to publish a summary of information received in the FEDERAL REGISTER at the close of the rebuttal period.

Dated: 9/30/80.

Edwin L. Johnson

Deputy Assistant Administrator
for Pesticide Programs

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